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Supplemental Material

Drivers of and Obstacles to the Adoption of Toxicogenomics for Chemical Risk Assessment: Insights from Social Science Perspectives

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Table S1: Quality control criteria employed in this study

This table synthesizes applicable criteria from the Equator Network: O'Brien et al.'s (2014) 'standards for reporting qualitative research (SRQR)', Tong et al.'s (2007, 2012) 'consolidated criteria for reporting qualitative studies (COREQ)' and 'enhancing transparency in reporting the synthesis of qualitative research (ENTREQ)', Clark's (2003) 'Relevance, Appropriateness, Transparency, and Soundness (RATS)' criteria, and Malterud's (2001) qualitative research standards.

Criteria & associated questions	*Answer*
Domain 1: Relevance of study question	
Is it important for medicine or public health?	Yes. Our research questions relate to the challenge of assessing tens of thousands of data-poor chemicals and understanding why the adoption of alternative testing strategies by regulators is taking more time than expected.
Is it justified and linked to existing knowledge base (literature, theory, practice)?	Yes. The rationale for our research questions is explicitly grounded in extant research.
Domain 2: Appropriateness of qualitative method	
Is qualitative methodology the best approach for the study aims?	Yes. A qualitative study is the most appropriate method to build a comprehensive compendium of drivers and obstacles to the adoption of toxicogenomics; and the most appropriate approach to interrogating these drivers and obstacles through the lenses of established frameworks addressing the adoption of innovations.
Why was a particular method chosen?	We analyzed the contents of published articles and documents produced by the toxicology and/or regulatory community to ensure that our sources and the drivers and obstacles we extracted from them reflect the concepts and vocabulary of these communities.
Domain 3: Research team and reflexivity	
Credentials – What were the research team's credentials? E.g. PhD, MD	All seven team members involved in data collection and analysis hold PhDs. Five are Associate Professors or Full Professors.
Occupation – What was their occupation at the time of the study?	Two postdoctoral researchers and five tenured professors.
Experience and training – What experience or training did the researcher have?	All team members are trained toxicology, management, and policy scientists. Team members involved in data collection and analysis total 60+ years of cumulated qualitative research experience.
Do the researcher(s) critically examine their own influence on the formulation of the research question, data collection, and interpretation?	Yes. Social scientists purposely conducted this study and leveraged established frameworks addressing the adoption of innovations to provide guidance to the natural scientists promoting new toxicogenomics tools.
Do the researchers occupy dual roles (clinician and researcher)?	No. All team members are researchers. None are clinicians.
Was trustworthiness of data checked?	Yes. Coders and auditors met regularly during the study to verify data collection and analysis, with emphasis on codes, categories, and findings.
Was an audit trail or triangulation employed?	Yes. In addition to the audit meetings above, the team employed triangulation across multiple data sources: multiple references support all codes and categories.
Are findings presented with reference to existing theoretical and applied literature?	Yes. One key purpose of the study was to relate the literature on toxicogenomics adoption with established innovation adoption frameworks. In turn, these theories

	feed into all findings, which convey practical implications for the adoption of toxicogenomics and other alternative testing strategies.
Domain 4: Data collection	
Methodological orientation and Theory – What methodological orientation was stated to underpin the study? E.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	We employed open coding (as used in grounded theory building) to identify key categories of drivers and obstacles to toxicogenomics adoption, which we then interpreted in light of established frameworks addressing the adoption of innovations.
Source selection - How were sources selected? Are criteria for data collection explained and justified? Was collection of data systematic and comprehensive?	We explain source selection, data collection and inclusion criteria in detail in the methods section.
Domain 5: Analysis and findings	
Derivation of themes – Were themes identified in advance or derived from the data? How were themes derived from the data?	We detail data analysis in the methods section. We derived categories of drivers and obstacles from the data, using concepts and vocabulary of the toxicology community. We then interrogate these findings using pre-established concepts from frameworks of innovation adoption that are widely used in the social sciences.
Were negative or deviant cases analysed?	Yes. We included all special cases in the study.
Were alternative explanations sought?	Yes. Alternative explanations are a central contribution of this study. We first present drivers and obstacles in the concepts and vocabulary of the toxicology community, then analyze them through the perspectives of two different established frameworks addressing the adoption of innovations.
Are the interpretations clearly presented and adequately supported by the evidence?	Yes. Interpretations are presented in the results section.
Reporting - Quotes presented – Were quotes presented to illustrate the themes / findings? Was each quotation identified?	Yes. We use referenced quotes to clarify our inclusion criteria for drivers and obstacles. We selected quotes based on how illustrative they are.
Reporting - Data and findings consistency – Was there consistency between the data presented and the findings?	Yes. We have detailed our analysis in the methods section so that readers can track the process linking data to findings.
Reporting - Clarity of major categories – Were major categories clearly presented in the findings?	Yes. Major categories are clearly presented in the form of the most salient drivers and obstacles.
Reporting - Clarity of minor categories – Is there a description of diverse cases or discussion of minor categories?	Yes. Minor categories are mentioned and minimally described in the form of the least salient drivers and obstacles.

Table S2: Peer-reviewed journals included in data collection

Alternatives to Animal Experimentation

American Journal of Public Health

Aquatic Toxicology

Archives of Toxicology

Big Data & Society

Biological Conservation

Critical Reviews in Toxicology

Drug Discovery Today

Ecotoxicology

Ecotoxicology and Environmental Safety

Environmental Health Perspectives

Environmental Politics

Environmental Science & Policy

Environmental Science and Pollution Research

Environmental Science & Technology

Environmental Toxicology and Chemistry

European Journal of Pharmaceutics and Biopharmaceutics

European Journal of Public Health

European Journal of Risk Regulation

Expert Opinion on Drug Safety

Governance: An International Journal of Policy, Administration, and Institutions

Harvard Environmental Law Review

Health, Risk & Society

Human and Ecological Risk Assessment: An International Journal

Integrated Environmental Assessment and Management

International Journal of Toxicology

Journal of European Public Policy

Journal of Nanoparticle Research

Journal of Pharmacogenomics & Pharmacoproteomics

Journal of the American Water Resources Association

Journal of Toxicology and Environmental Health

Molecular Carcinogenesis

Mutation Research - Fundamental and Molecular Mechanisms of Mutagenesis

Nature

Nature Biotechnology

Nature Genetics

Nature Reviews Genetics

Nucleic Acids Research

Pharmacogenomics

Progress in Biophysics & Molecular Biology

Pure and Applied Chemistry

Regulatory Toxicology and Pharmacology

Review of European, Comparative & International Environmental Law

Risk Analysis

Science

Science and Public Policy

Science of the Total Environment

Science, Technology, & Human Values

Social Studies of Science

Stanford Law Review

Technological Forecasting and Social Change

Technovation

The Social Science Journal

Toxicological Sciences

Toxicology

Toxicology in Vitro

Toxicology Letters

Toxicology Research

Trends in Biotechnology

Trends in Pharmacological Sciences

Yale Journal on Regulation

Table S3: Books included in data collection

Ankley GT, Miracle AL, Perkins EJ, Daston GP, eds. 2008. Genomics in regulatory ecotoxicology: Applications and challenges. CRC Press ; SETAC: Boca Raton; Pensacola, FL.

Burczynski ME, ed. 2003. An introduction to toxicogenomics. CRC Press: Boca Raton, FL.

Eskes C, Whelan M, eds. 2016. Validation of alternative methods for toxicity testing. Springer:Switzerland.

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Mendrick DL, Mattes WB, eds. 2008. Essential concepts in toxicogenomics. Humana Press, Springer: Totowa, NJ.

Salem H, Katz SA. 1999. Toxicity assessment alternatives: Methods, issues, opportunities. Humana Press, Springer: Totowa, NJ.

Sharp RR, Marchant GE, Grodsky JA. 2008. Genomics and environmental regulation: Science, ethics, and law. Johns Hopkins University Press: Baltimore, MD.

Table S4: Authoritative national sources, specialized associations, and international institutions included in data collection

AltTox.org	Interagency Coordinating Committee on the Validation of Alternative Methods	United Nations Environment Programme
Chemical Watch	International Labour Organization	US Food and Drug Administration
Environment and Climate Change Canada	NTP Interagency Center for the Evaluation of Alternative Toxicological Methods	US Environmental Protection Agency
European Centre For Ecotoxicology and toxicology of Chemicals	Organisation for Economic Co-operation and Development	US National Academies of Sciences, Engineering, and Medicine
European Centre for the Validation of Alternative Methods	Public Health England	US National Institutes of Health
European Chemicals Agency	Society for Environmental Toxicology and Chemistry	US National Institute of Environmental Health Sciences
European Commission	Society for Risk Analysis	US National Research Council
Government of Canada	Society of Toxicology	US National Toxicology Program
Health Canada		World Health Organization
Human Toxicology Project Consortium		

Table S5: Sources making up the corpus of texts analyzed

Andersen ME, Krewski D. 2010. The Vision of Toxicity Testing in the 21st Century: Moving from Discussion to Action. Toxicological Sciences 117:17–24; doi:10.1093/toxsci/kfq188.

Ankley G, Daston GP, Degitz SJ, Denslow ND, Hoke RA, Kennedy SW, et al. 2006. Toxicogenomics in Regulatory Ecotoxicology. Environmental Science & Technology 40: 4055–4065.

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Chen M, Zhang M, Borlak J, Tong W. 2012. A Decade of Toxicogenomic Research and Its Contribution to Toxicological Science. Toxicological Sciences 130:217–228; doi:10.1093/toxsci/kfs223.

Dunn RT, Kolaja KL. 2003. Gene Expression Profile Databases in Toxicity Testing. In: An Introduction to Toxicogenomics (M.E. Burczynski, ed). Informa Healthcare, CRC Press: Boca Raton, FL. 213–224.

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ECHA (European Chemicals Agency). 2016. Topical Scientific Workshop on New Approach Methodologies in Regulatory Science - Background document. ECHA: Helsinki, FI. 19 pp.

ECVAM (European Centre for the Validation of Alternative Methods), ICCVAM (Interagency Coordinating Committee on the Validation of Alternative Methods). 2003. Workshop on the Validation Principles for Toxicogenomics-Based Test Systems: An overview. ECVAM: Ispra, IT. 5 pp.

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Table S6: First, median, and last year of mention of drivers and obstacles

Year	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
# of sources in corpus of texts	0	1	1	3	2	5	3	5	4	5	1	4	5	1	2	0	1	3	4	6	**56**
Drivers																					
D1	0	0	0	2	2	2	1	2	1	3	1	3	3	2	1	0	0	2	1	0	**26**
D2	0	0	1	2	0	2	1	2	1	1	1	2	1	2	1	0	0	1	1	1	**20**
D3	0	0	1	2	0	1	0	1	1	2	0	1	1	0	1	0	0	1	2	2	**16**
D4	0	0	0	1	1	0	0	1	1	3	0	1	0	1	2	0	0	2	0	0	**13**
D5	0	0	1	1	1	3	0	2	0	2	0	1	0	0	0	0	0	1	0	0	**12**
D6	0	0	1	0	0	0	0	1	1	1	0	0	1	1	1	0	0	1	1	0	**9**
D7	0	0	0	1	0	1	0	0	0	0	0	1	1	1	0	0	0	1	0	0	**6**
D8	0	0	0	1	1	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	**5**
D9	0	0	0	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	1	0	**4**
D10	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	**2**
D11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	**1**
Total	**0**	**0**	**4**	**10**	**5**	**9**	**3**	**10**	**7**	**14**	**3**	**9**	**7**	**8**	**6**	**0**	**0**	**10**	**6**	**3**	**114**
Obstacles																					
O1	0	1	0	1	0	3	1	3	3	4	1	3	2	1	0	0	1	1	2	6	**33**
O2	0	0	1	1	0	2	2	3	2	2	0	2	2	1	1	0	0	0	2	1	**22**
O3	0	0	0	0	0	1	1	3	3	2	1	0	2	1	0	0	0	1	2	3	**20**
O4	0	1	0	1	0	1	0	3	1	0	0	0	0	1	0	0	0	1	1	2	**12**
O5	0	0	0	0	0	0	0	2	0	0	1	2	1	0	0	0	0	2	1	1	**10**
O6	0	0	0	0	0	0	0	2	1	2	0	1	1	0	0	0	0	0	0	1	**8**
O7	0	0	0	0	0	1	0	2	1	1	0	1	0	1	0	0	0	0	0	0	**7**
O8	0	0	0	0	0	0	0	1	1	1	0	1	1	0	0	0	0	0	0	1	**6**
O9	0	0	0	0	0	0	0	1	0	0	0	1	1	0	0	0	0	0	1	0	**4**
O10	0	0	0	0	0	0	0	0	0	1	0	0	2	0	0	0	0	0	0	1	**4**
O11	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	**2**
O12	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	**2**
Total	**0**	**2**	**1**	**3**	**0**	**9**	**5**	**20**	**12**	**13**	**4**	**11**	**13**	**5**	**1**	**0**	**1**	**5**	**9**	**16**	**130**

Key: First year of mention; Median year of mention; Last year of mention

Notes:

Drivers

D1) Superior scientific understanding: Omics methods allow for a better understanding of health and ecological effects from exposures to chemicals

D2) New applications: Omics methods offer new applications in human and ecological toxicology

D3) Reduced cost & increased efficiency: Omics methods will reduce the cost and time, increase the efficiency and scale of testing

D4) Scientific and technological advances: Scientific and technological advances enhance the capacity of omics methods to improve scientific understanding and generate new applications in toxicology
D5) Belief in the potential of omics: Field actors express their belief in the potential and promise of omics methods
D6) Stakeholder commitment & investment: Government and industry are committed to, and invest in, the development of omics methods
D7) Reduced animal use: Omics methods are expected to reduce animal use in toxicity testing
D8) Numerous untested chemicals: The high number of untested incumbent and new chemicals creates pressure for adopting new testing approaches
D9) Enabling laws & regulations: New laws and regulations convey directions that foster omics methods
D10) Accessibility of capabilities & resources: Omics tools and expertise are becoming more available
D11) International collaboration & harmonization: International collaboration supports the harmonization of omics methods

Obstacles
O1) Insufficient validation: Omics methods are insufficiently validated, especially for regulatory uses
O2) Complexity of interpretation: Interpretation of omics data is complex and needs clearer links to biological impacts
O3) Lack of standardization: Omics methods need standardization
O4) Lack of expertise: Field actors lack expertise and need training
O5) Difficulty of coordination: The efforts of field actors lack coordination. Technical and IP rights issues with data sharing hinder coordination
O6) Resistance to change: Field actors resist the use and adoption of omics methods
O7) High level of required investment: Using omics requires significant investment
O8) Lack of organizational support: There is a lack of funding, resources, and organizational support for omics methods
O9) Uncertain economic benefits: The economic benefits of omics are uncertain
O10) Inadequacy for some applications: There are some areas of toxicology where omics cannot be applied
O11) Concerns about litigation: Actors are concerned with litigation from retrospective analysis
O12) Frustrated expectations: Omics created unrealistic expectations which are not fulfilled

SUPPLEMENTAL MATERIAL – REFERENCES

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